Fig. 1

## Fig 2. cout.

210 215 220 222 225 228 232 C N V N H K P S N T K V D K K V E P K S TGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAAGTTGAGCCCAAATCT 778 HINGE⇒

235 240 245 250 C D K T H T C P P C P A P E L L G G P S TGTGACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCA 838  $C_{\mu}2\Rightarrow$ 

255 260 265 270
V F L F P P K P K D T L M I S R T P E V
GTCTTCCTCTTCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTC 898

275 280 285 290 292 T C V V V D V S H E D P E V K F N W Y V ACATGCGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTG 958

295 299 300 305 314 317
D G V E V H N A K T K P R E E Q Y N S T
GACGGCGTGGAGGTGCATAATGCCAAGACAAGCCGCGGGAGGAGCAGTACAACAGCACG 1018

320 325 330 335
Y R V V S V L T V L H Q D W L N G K E Y
TACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTAC 1078

340 345 350 355 357

K C K V S N K A L P A P I E K T I S K A

AAGTGCAAGGTCTCCAACAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCC 1138

360 363 365 370 375 378 381 
K G Q P R E P Q V Y T L P P S R D E L T 
AAAGGGCAGCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACC 1198  $C_{H}3\Rightarrow$ 

385 390 395 400 402 K N Q V S L T C L V K G F Y P S D I A V AAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTG 1258

405 408 410 414 415 420 425 E W E S N G Q P E N N Y K T T P P V L D GAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGAC 1318

430 433 435 440 445 450 S D G S F F L Y S K L T V D K S R W Q Q TCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAG 1378

455 460 465 470
G N V F S C S V M H E A L H N H Y T Q K
GGGAACGTCTCCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAG 1438

Fig.2

TCTAAAGAAGCCCCTGGGAGCACAGCTCATCACCATGGACTGGACCTGGAGGTTCCTC 58 SIGNAL⇒ TTTGTGGTGCAGCAGCTACAGGTGTCCAGTCCCAGATGCAGGTGGTGCAGTCTGGGGGCT 118 FR1⇒ GAAGTAAAGAAGCCTGGGTCCTCGGTGACGGTCTCCTGCAAGGCATCTGGAGGCACCTTC 178 33 34 35 40 I S W V R Q AGCAACTATGCTATCAGCTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGA 238 CDR1⇒ FR2⇒ 50 51 52 a 53 54 55 56 57 58 59 60 61 62 63 64 65 G T PTYSQN GGGATCATCCCTCTTTTTGGTACACCAACCTACTCACAGAACTTCCAGGGCAGAGTCACG 298 CDR2⇒ FR3⇒ 70 80 82 a b c 83 TADKSTSTAHMELTSLR ATTACCGCGGACAAATCCACCAGCACAGCCCACATGGAGCTGACTAGCCTGAGATCTGAG 358 90 95 96 97 98 99 100 a A V Y Y C A T D R Y R Q A N CDR3⇒ f g h i k 101 102 105 110 RVGWFDPW G Q G T L V T V S S A S CGGGTTGGCTGGTTCGACCCCTGGGCCCAGGGCACCCTGGTCACCGTCTCCTCAGCCTCC 478 FR4⇒  $C_{H}1 \Rightarrow$ 120 125 130 133 SVFPLAPSSKS ACCAAGGCCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACA 538 145 150 154 156 162 A A L G C L V K D Y F P E P V T V S W N GCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAAC 598 165 169 171 175 180 182 SGALTSGVHTFPAVLQSGL TCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTC 658 190 195 200 203 205 185

Y S L S S V V T V P S S S L G T Q T Y I

TACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATC 718

CAAGAGGCAGCGCTCTCGGGACGTCTCCACCATGGCCTGGGCTCTGCTGCTCCTCACC 58 SIGNAL⇒ FR1⇒ 15 20 24 25 26 27 d e f 28 S G S P G Q S I T I S C T G T N N D V G TCTGGGTCTCCTGGACAGTCGATCACCATCTCCTGCACTGGAACCAACAATGATGTTGGG 178 CDR1⇒ 29 30 31 32 33 34 35 40 V S W Y Q Q H P G K A AGTTATAACCTTGTCTCCTGGTACCAGCAGCACCCCAGGCAAAGCCCCCAAAATCATGATT 238 FR2⇒ 50 51 52 53 54 55 56 60 Y E V S K R P S G V S N R F S G S K S G TATGAGGTCAGTAAGCGGCCCTCAGGGGTTTCTAATCGCTTCTCTGGCTCCAAGTCTGGC 298 CDR2⇒ FR3⇒ 70 75 80 NTASLTISGLQAEDEADYYC AACACGGCCTCCCTGACAATCTCTGGGCTCCAGGCTGAGGACGAGGCTGATTATTACTGC 358 89 90 91 92 93 94 95 a 96 97 100 C S Y A G S Y TVVFGGGK TGCTCATATGCAGGTAGTTACACTGTGGTTTTTCGGCCGAGGGACCAAACTGACCGTCCTA 418 CDR3⇒ FR4⇒ 107 110 115 120 G Q P K A A P S V T L F P P S S E E L Q GGTCAGCCCAAGGCTGCCCCCTCGGTCACTCTGTTCCCGCCCTCCTCTGAGGAGCTTCAA 478 C<sub>l</sub>⇒ 130 140 K A T L V C L I S D F Y P G A V T V GCCAACAAGGCCACACTGGTGTCTCATAAGTGACTTCTACCCGGGAGCCGTGACAGTG 538 150 155 160 AWKADSSPVKAGVETTTP GCCTGGAAGGCAGATAGCAGCCCCGTCAAGGCGGGAGTGGAGACCACCACACCCTCCAAA 598

Q S N N K Y A A S S Y L S L T P E Q W K CAAAGCAACAACAACAGCGGCCAGCAGCTATCTGAGCCTGACGCCTGAGCAGTGGAAG 658

190 195 200 203 205
S H R S Y S C Q V T H E G S T V E K T V TCCCACAGAAGCTACAGCTGCCAGGTCACGCATGAAGGGAGCACCGTGGAGAAGACAGTG 718

180

175

## APP DE LO MANTE DE LA CA

Fig 3. cont.

GACATCCAGATCACCAGTCTCCATCCTCCATCTGAGACACAGAGTCACCATCATCGCGGGCAAGTCAG TC
Human Cynok1 Cynok2 Cynok1 Cynok2 Cynok1 Cynok2 Cynok1 Cynok2 Cynok1 Cynok1 Cynok1 Cynok2 Cynok1 Cynok2 Cynok2 Cynok1 Cynok1 Cynok1 Cynok1 Cynok1 Cynok1 Cynok2 Cynok1 Cynok2 Cynok1 Cynok2 Cynok1 Cynok1 Cynok1 Cynok1 Cynok1 Cynok1 Cynok1 Cynok1 Cynok2 Cynok1 Cynok1 Cynok2 Cyn

Fig. 4 cont.

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	1 C		AG-AA		C-AA				<u>G</u>			GGACACGACTGGA	CAA-G	CAAGG	CAAGG		CAA-G	CAAGG	CAA	CAA-G	CAAGG	CAAGG	CGAG	CAAG
70		B	-ACT	L>	1	B	B	G-A	T	***	100	TCACCTTCGGCCAAG	AGTTG-	L	L	GGG	AGTTG-	B95	TCC-	AGTTG-	TGG		CTG-TGG	GTGCT-
ZAGTGGCAGTGGATC	CC		C	C	9			AA		CDR3	95 a		GAC- T	E	GCT C-	C-GT-T-CT T	_OÐ	GT-T-CT CC	ACAC-TT-CA T-	-C-TACA T	AT-C	TA	GTAGCGAT	CTAT-CT C-
60 GTCACATCAAGGTTC	TC-C-TC-		CGAC	C	CGAC		C		>T&&T->	*****	90	<b>TGTCAACAGAGTTAC</b>		G	GT-A1	GAGC-CT	9	$\overline{}$	-AC	CGTA-A-T	GA-	ATA-A-	<b>-</b>	GCTT
CAAAGTGGGGT				GA	GCCTCA	9	G	GC-TC				CTTA	GTT		L	GTT		A	GTT		- - - - - - - - -	·		CAT
Human	CynoKl	CynoK4	CynoK5 CvnoK9		CynoK14	4 -4	2	Rabbit	Mouse			Human	CynoK1	CynoK2	CynoK4	CynoK5	CynoK9	CynoK12	CynoK14	CynoK15	CynoK18	CynoK20	Rabbit	Mouse

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Fig. 5

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Fig. 5. cont.

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130 GAAATCTGGAACTGCCTC TTA-T-A-	150  TACAGTGGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCCAGGAGTGTCACAGAGCAGGACAGC A	190 CTACGAGAACACAAGTCTA( CGTGC	
120 CTTCATCTTCCGCCATCTGAGGAGTT 	150 AGTACAGTGGAAGGTGGATAACGCCCTCCA 3CAGGTA-GGAAA-G-AGTGAA-G	180 CAGCACCCTGACGCTGAGCAAAGCAGA -6GCA- <u>A</u> CCCCCC	200 CAGGGCCTGAGCTCGCCCGTCACAAGAGCTTCAACAGGGGAGAGTGTTAG 
	140 TTCTATCCCAGAGGCCAAAGTACAG GCATCATCAC-CACC		-
Human Cynomolgus Rabbit	Human Cynomolgus Rabbit Mouse	Human Cynomolgus Rabbit Mouse	Human Cynomolgus Rabbit Mouse

Fig.7.

- G B - G S - G S S - G S S	H	
250 W K V K - K - K T K I	H H H	
E A E C C C C C C C C C C C C C C C C C	190 K H K L S I N V R I S V	-
140 N F Y P R I I I I I K I R I K	K A D K E L D H D D L N D E L L D E L L L L L L L L L L L L L L	
C I I I I I I I I I I I I I I I I I I I	180 L T L S - - S - T -	
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L K S G I I I I I I I I I I I I I I I I I I	170 D S T Y - N - C	4
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A P S	160 G N S Q D S G I E N G V L	S S P C C T C T T T T T T T T T T T T T T T
110 T V A gus A D P I A D -	L Q S gus - K T I - Q E R Q	200 200 3us K T S
Human Cynomolgus Rabbit Mouse	Human Cynomolgus Rabbit Mouse	Human Cynomolgus Rabbit Mouse

Fig.2

-19
M D W T W R F L
TCTAAAGAAGCCCCTGGGAGCACAGCTCATCACC<u>ATGGACTTGGACCTGGAGGTTCCTC</u> 58
SIGNAL⇒

F V V A A A T G V Q S Q M Q V V Q S G A

TTTGTGGTGCAGCTACAGGTGTCCAGTCCCAGATGCAGGTGGTGCAGTCTGGGGCT 118
FR1⇒

10 15 20 25
E V K K P G S S V T V S C K A S G G T F
GAAGTAAAGAAGCCTGGGTCCTCGGTGACGGTCTCCTGCAAGGCATCTGGAGGCACCTTC 178

30 31 32 33 34 35 40 45
S N Y A I S W V R Q A P G Q G L E W M G
AGCAACTATGCTATCAGCTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGA 238
CDR1⇒ FR2⇒

50 51 52 a 53 54 55 56 57 58 59 60 61 62 63 64 65
G I I P L F G T P T Y S Q N F Q G R V T

GGGATCATCCCTCTTTTTGGTACACCAACCTACTCACAGAACTTCCAGGGCAGAGTCACG 298
CDR2⇒
FR3⇒

70 75 80 82 a b c 83 85 I T A D K S T S T A H M E L T S L R S E ATTACCGCGGACAAATCCACCAGCACAGCCCACATGGAGCTGACTAGCCTGAGATCTGAG 358

f g h i k 101 102 105 110 115 R V G W F D P W G Q G T L V T V S S A S CGGGTTGGCTGGTCGCCCCTGGGGCCAGGGCACCCTGGTCACCGTCTCCTCAGCCTCC 478  $C_{u}1\Rightarrow$ 

120 125 130 133 135
T K G P S V F P L A P S S K S T S G G T
ACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACA 538

140 145 150 154 156 162 A A L G C L V K D Y F P E P V T V S W N GCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAAC 598

165 169 171 175 180 182 S G A L T S G V H T F P A V L Q S S G L TCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTC 658

185 190 195 200 203 205
Y S L S S V V T V P S S S L G T Q T Y I
TACTCCCTCAGCAGCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATC 718

## 5001 0 30 10 montes

210 215 220 222 225 228 232 C N V N H K P S N T K V D K K V E P K S TGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAAAGTTGAGCCCAAATCT 778 HINGE⇒

235 240 245 250 C D K T H T C P P C P A P E L L G G P S TGTGACAAACTCACACATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCA 838  $C_{\rm H}2\Rightarrow$ 

255 260 265 270 V F L F P P K P K D T L M I S R T P E V GTCTTCCTCTTCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTC 898

275 280 285 290 292 T C V V V D V S H E D P E V K F N W Y V ACATGCGTGGTGGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTG 958

295 299 300 305 314 317
D G V E V H N A K T K P R E E Q Y N S T
GACGGCGTGGAGGTGCATAATGCCAAGACAAGCCGCGGGAGGAGCAGTACAACAGCACG 1018

320 325 330 335
Y R V V S V L T V L H Q D W L N G K E Y
TACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTAC 1078

340 345 350 355 357

K C K V S N K A L P A P I E K T I S K A

AAGTGCAAGGTCTCCAACAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCC 1138

360 363 365 370 375 378 381 K G Q P R E P Q V Y T L P P S R D E L T AAAGGGCAGCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACC 1198 C<sub>H</sub>3⇒

385 390 395 400 402 K N Q V S L T C L V K G F Y P S D I A V AAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTG 1258

405 408 410 414 415 420 425 E W E S N G Q P E N N Y K T T P P V L D GAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGAC 1318

430 433 435 440 445 450 S D G S F F L Y S K L T V D K S R W Q Q TCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAG 1378

455 460 465 470
G N V F S C S V M H E A L H N H Y T Q K
GGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAG 1438

FIG 3

-19

M A W A L L L T
CAAGAGGCAGCGCTCTCGGGACGTCTCCACCATGGCCTGGGCTCTGCTCCTCACC 58
SIGNAL⇒

29 30 31 32 33 34 35 40 45
S Y N L V S W Y Q Q H P G K A P K I M I

AGTTATAACCTTGTCTCCTGGTACCAGCAGCACCCAGGCAAAGCCCCCAAAATCATGATT 238
FR2⇒

50 51 52 53 54 55 56 60 65 Y E V S K R P S G V S N R F S G S K S G TATGAGGTCAGTAAGCGGCCCTCAGGGGTTTCTAATCGCTTCTCTGGCTCCAAGTCTGGC 298 CDR2 $\Rightarrow$  FR3 $\Rightarrow$ 

70 75 80 85 N T A S L T I S G L Q A E D E A D Y Y C AACACGGCCTCCCTGACAATCTCTGGGCTCCAGGCTGAGGACGAGGCTGATTATTACTGC 358

89 90 91 92 93 94 95 a 96 97 100 106 a
C S Y A G S Y T V V F G G G T K L T V L

TGCTCATATGCAGGTAGTTACACTGTGGTTTTTCGGCGGAGGGACCAAACTGACCGTCCTA 418
CDR3⇒
FR4⇒

107 110 115 120 125
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130 135 140 145 A N K A T L V C L I S D F Y P G A V T V GCCAACAAGGCCACACTGGTGTCTCATAAGTGACTTCTACCCGGGAGCCGTGACAGTG 538

150 155 160 165 A W K A D S S P V K A G V E T T T P S K GCCTGGAAGGCAGATAGCAGCCCCTCAAAGGCGGGAGTGGAGACCACCACCCTCCAAA 598

168 170 175 180 185 Q S N N K Y A A S S Y L S L T P E Q W K CAAAGCAACAAGTACGCGGCCAGCAGCTATCTGAGCCTGACGCCTGAGCAGTGGAAG 658

190 195 200 203 205 S H R S Y S C Q V T H E G S T V E K T V TCCCACAGAAGCTACAGCTGCCAGGTCACGCATGAAGGGAGCACCGTGGAGAAGACAGTG 718



Fig 3. cont.

			Fig. 4 cont.	
80 AGCAGTCTGCAACCTGAAGATTCTGCA	99999999	C	GAGATTAAA CCGA CGA CGA	
70 SACTTCACTCTCACCATC	T	TTTTTTT	100 3GCCAAGGGACACGACTG GCAAGGGGCAAGG	G
GCAGTGGATCTGGGACA		GGGGGGG	3 ****** CCCTG ACT ACT CT	C- TAGTT -T-CT CGGGTCA TAGTT -AT-CT CCGGGTAGCGAT-CTG-TAT-CT CCGG
60 TCACATCAAGGTTCAG	A-TC-C-TC	GAC	CD ************************************	TTTGTGTTCATGATA-ACACACT
_	CynoKl CynoK4 CynoK5	Cynok12 Cynok14 Cynok15 Cynok18 Cynok20 Cynok20 Cynok20 Cynok20 Cynok20 Cynok20	Human ACTT CynoK1 GT CynoK2 CynoK4 CynoK5 GT	CynoK12 CynoK14 CynoK15 CynoK18 CynoK18 CynoK20 CynoK20 Rabbit Rabbit Mouse CA

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Fig. 5. cont.

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	Human		TCCCGCCATCTGATGAGCAGTTGAAA	ACTGTGCTGCTCTTCTTCTTCTTCCCGCCATCTGAGGAGTTGAAATCTGGAACTGCTTGTTGTGTGCTTGTTGTTGTTGTTGTTGTTAATAAC
	Cynomolgus Rabbit	GA-CCAATGTA		T
	Mouse	6A'I'	ACAGA-C	-99
	Human		GGAAGGTGGATAACGCCCTCCAATCC	TTCTATCCCAGAGGCCAAAGTACAGTGGATAACGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCACAGAGCAGGACAGC
	Cynomolgus Rabbit Mouse	CGATCATCCCACC	GGTCA	AACA
•		170	180	190
	Human	<del>-</del>	CCCTGACGCTGAGCAGACTACGAGAACA	ပေ၊
•	Rabbit	G-AT-T-TA	-TT-ACC-GA-C-GC	GCT
	Human	210 CAGGCCTGACACAAAGAGCTTCAAGAGAGAGAGAGTTAAG	210 GCTTCAACAGGGGAAGTGTTAG	
	Cynomolgus			
	Rabbit	CAA-TC-GAG-GAGTCC	C	

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